IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

BIOVAIL CORPORATION,	)	
	)	
and	)	
	)	
BIOVAIL LABORATORIES INTERNATIONAL, SRL,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	8:06-cv-03355-RWT
	)	
UNITED STATES FOOD AND DRUG ADMINISTRATION,	)	
	)	
and	)	
	)	
ANDREW C. VON ESCHENBACH, M.D., in his official capacity as COMMISSIONER OF FOOD AND DRUGS,	)	
	)	
Defendants,	)	

GOVERNMENT'S OPPOSITION TO PLAINTIFFS' MOTION FOR
A TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION

INTRODUCTION

At issue in this case is the approval by the United States Food and Drug Administration (FDA or agency) of a generic version of 300 mg buproprion hydrochloride (HCl) extended-release tablets, an antidepressant. Biovail Corporation (Biovail) manufactures the brand-name version of bupropion HCl extended-release tablets for GlaxoSmithKline (GSK), which markets the drug as Wellbutrin XL®. IMPAX Laboratories, Inc. (IMPAX) submitted to FDA an application to manufacture and sell generic versions of Wellbutrin XL in 150 mg and 300 mg dosage strengths. On December 14, 2006,FDA approved IMPAX's application for the 300 mg

dosage of generic Wellbutrin, and Biovail filed suit for temporary and preliminary injunctive relief staying FDA's approval of IMPAX's application.

Biovail has benefitted from a monopoly on this product, which it seeks to perpetuate with this lawsuit. FDA's decision to approve IMPAX's Abbreviated New Drug Application (ANDA) to manufacture and sell 300 mg dosages of generic bupropion HCl extended-release tablets is required by the Federal Food, Drug, and Cosmetic Act (FDCA) and is not arbitrary or capricious. Biovail's attempt to reverse this decision in order to prolong its monopoly, while decreasing the availability of low cost, reliable, and safe pharmaceuticals, should be rejected.

Biovail does not meet the standard for a preliminary injunction because it has no likelihood of success on the merits of its case. Further, Biovail will not suffer irreparable injury from the denial of preliminary injunctive relief pending resolution of this action on the merits.

Because the alleged harm that Biovail will suffer if a preliminary injunction is not granted is far less than what the public, FDA, and IMPAX (and any other party with an approved or pending ANDA for a generic version of 300 mg Wellbutrin XL) will suffer if one is granted, the balance of harms weighs against Biovail in this case. For this reason, Biovail must establish a very strong likelihood that FDA's approval of generic 300 mg bupropion HCl extended-release tablets must be set aside – a burden Biovail has manifestly failed to meet.

Specifically, Biovail alleges that FDA's approval of IMPAX's ANDA for the 300 mg dosage was unlawful because Biovail allegedly filed a timely lawsuit for patent infringement, which required FDA to stay its approval of IMPAX's ANDA for 30 months or until the completion of the patent litigation. Although Biovail filed a timely patent lawsuit on the 150 mg strength, Biovail did not file its patent lawsuit on the 300 mg strength Wellbutrin XL within the

45 days required by the FDCA, and therefore, is not entitled to a 30 month stay on approval of IMPAX's generic of that strength. Moreover, Biovail recognized its failure when it amended – 30 days too late – its first patent suit to include the 300 mg strength.

For all of these reasons, FDA's decision should be upheld, and Biovail's motion for a temporary restraining order and preliminary injunction should be denied.

STATEMENT OF THE CASE

I. STATUTORY AND REGULATORY SCHEME

A. New Drug Applications

FDA approves applications to market drugs under the FDCA, 21 U.S.C. § 355. Under this provision, pharmaceutical companies seeking to market "pioneer" or "innovator" drugs must first obtain FDA approval by filing a new drug application (NDA) containing extensive scientific data demonstrating the safety and effectiveness of the drug. 21 U.S.C. § 355(a), (b). An NDA applicant must also submit information on any patent that claims the drug or a method of using the drug and for which a claim of patent infringement could reasonably be asserted against an unauthorized party. 21 U.S.C. § 355(b)(1), (c)(2). FDA publishes the patent information it receives in "Approved Drug Products With Therapeutic Equivalence Evaluations" (the "Orange Book"). Id.; see also 21 U.S.C. § 355(j)(7); 21 C.F.R. § 314.53(e); Declaration of Martin H. Shimer ("Shimer Dec.") attached at Exh. 1. FDA listed as a separate drug product the 150mg and 300 mg strengths separately in the Orange Book.

B. Abbreviated New Drug Applications ("ANDAs")

The Drug Price Competition and Patent Term Restoration Act of 1984 (known as the "Hatch-Waxman Amendments"), codified at 21 U.S.C. §§ 355, 360cc and 35 U.S.C. §§ 156,

271, 282, permits the submission of ANDAs for approval of generic versions of approved drug products. 21 U.S.C. § 355(j). The ANDA process shortens the time and effort needed for approval by, among other things, allowing the applicant to demonstrate its generic product's bioequivalence to a drug product already approved under an NDA (the "listed" drug), rather than having to reproduce the safety and effectiveness data for that drug. Eli Lilly and Co. v. Medtronic, Inc., 496 U.S. 661, 676 (1990).[1] If an ANDA applicant establishes that its proposed drug product has the same active ingredient, strength, dosage form, route of administration, labeling, and conditions of use as a listed drug, and that it is bioequivalent to that drug, the applicant can rely on FDA's previous finding that the listed drug is safe and effective. See id. The FDCA sets forth in detail additional information that an ANDA must contain, and lists the numerous deficiencies that may prevent or delay approval of an ANDA. See 21 U.S.C. §§ 355(j)(2), 355(j)(4).

1. Patent Certifications

The timing of approval of ANDAs depends, in part, on patent protections for the pioneer drug. An ANDA must contain one of four specified certifications for each patent that "claims the listed drug" or "a use for such listed drug for which the applicant is seeking approval." 21 U.S.C. § 355(j)(2)(A)(vii). The certification must state one of the following:

> (I) that the required patent information relating to such patent has not been filed;
>
> (II) that such patent has expired;

[1] Two drugs are considered bioequivalent if, in general, the rate and extent of absorption of the proposed drug is not significantly different from the rate and extent of absorption of the listed drug. 21 U.S.C. § 355(j)(8)(B).

(III) that such patent will expire on a particular date; or

(IV) that such patent is invalid or will not be infringed by the drug for which approval is being sought.

See id.

If a certification is made under paragraph I or II indicating that patent information pertaining to the drug or its use has not been filed with FDA or the patent has expired, then the patent, by itself, will not delay approval of the ANDA. 21 U.S.C. § 355(j)(5)(B)(i). A certification under paragraph III indicates that the ANDA applicant does not intend to market the drug until after the applicable patent has expired, and FDA will not approve the ANDA until after the patent had expired. 21 U.S.C. § 355(j)(5)(B)(ii).

However, if an applicant wishes to challenge a patent's validity or to claim that the patent would not be infringed by the product proposed in the ANDA, as occurred in this case, the applicant must submit a separate paragraph IV certification to FDA for each product it seeks to market. The applicant must also provide notice of each paragraph IV certification to the NDA holder and the patent owner and describe the factual and legal basis for the applicant's opinion that the patent is invalid or not infringed. 21 U.S.C. § 355(j)(2)(B). The filing of a paragraph IV certification "for a drug claimed in a patent or the use of which is claimed in a patent" is an act of infringement. 35 U.S.C. § 271(e)(2)(A). This enables the NDA holder and patent owner to sue the ANDA applicant for each product it seeks to protect.

If the patent owner or NDA holder brings a patent infringement suit against the ANDA applicant within 45 days after receiving notice of the paragraph IV certification, the suit can trigger an automatic stay of FDA approval of the particular challenged product that is the subject of the certification and the lawsuit for 30 months from the date the patent owner or NDA holder

received notice of the certification ("30-month stay"). 21 U.S.C. § 355(j)(5)(B)(iii). The 30-month stay can be modified or lifted if the patent court reaches a decision before 30 months expires or otherwise orders a longer or shorter stay period.[2] Id. At the end of 30 months (or such shorter or longer period as the court orders), FDA will approve the ANDA in spite of the unexpired patent and ongoing litigation if the ANDA is otherwise ready for approval.

If, as occurred in this case, the patent owner or NDA holder does not bring suit within 45 days after it has received notice of the paragraph IV certification, the unexpired patent will not, by itself, bar FDA's approval of the ANDA, even if patent litigation is subsequently commenced outside the 45-day period and is ongoing at the time the requirements for approval are met. In that circumstance, FDA may approve the ANDA provided there are no other patent or exclusivity barriers to approval and the other conditions of approval are met. 21 U.S.C. § 355(j)(5)(B)(iii); 21 C.F.R. § 314.107(f)(2). FDA's approval of the ANDA does not affect the ongoing patent litigation, and the pioneer may still recover damages for infringement if it prevails in the patent litigation.

II. FACTUAL BACKGROUND

A. NDA for Wellbutrin XL

On August 28, 2003, FDA approved Wellbutrin XL as an extended-release formulation under NDA 21-515 in both 150- and 300-mg tablets. Both strengths of Wellbutrin XL tablets are approved for the treatment of major depressive disorder and for the prevention of seasonal major depressive episodes in patients with a diagnosis of seasonal affective disorder.

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[2] For instance, if the ANDA applicant prevails in the patent infringement litigation, the 30-month stay is lifted upon the district court's decision, and FDA can approve the ANDA in spite of any pending appeal (unless the court imposes a stay of approval while the appeal is pending).

B. IMPAX's ANDA for a generic version of Wellbutrin XL

On November 30, 2004, IMPAX submitted an ANDA for a generic version of 150 mg Wellbutrin XL to FDA. See Exh. 2. Along with its ANDA, IMPAX submitted a Paragraph IV Patent Certification, stating that patent numbers 6,096,341 and 6,143,327 are "invalid, unenforceable, or will not be infringed by the manufacture, use or sale of the bupropion HCL extended-release tablets, 150 mg." Id. (emphasis added). FDA assigned IMPAX's ANDA number 77-415.

On December 28, 2004, IMPAX submitted an amendment to ANDA 77-415, providing for the addition of a 300 mg strength bupropion HCl. See Exh. 3. Along with its ANDA, IMPAX submitted another Paragraph IV Patent Certification, also stating that patent numbers 6,096,341 and 6,143,327 are "invalid, unenforceable, or will not be infringed by the manufacture, use or sale of the bupropion HCL extended-release tablets, 300 mg." Id. (emphasis added).

By letter dated January 20, 2005, as required by 21 U.S.C. § 355(j)(2)(B)(ii), IMPAX gave Biovail notice of its Paragraph IV Certification with regard to its ANDA 77-415 seeking approval of its generic 150 mg extended release tablets (150 mg Notice). See Plaintiffs' Memorandum of Points and Authorities in Support of Plaintiffs' Motion for a Temporary Restraining Order and Preliminary Injunction (PI Mem.) at 5-6. Biovail received the 150 mg Notice on January 24, 2005. Id. By letter dated January 24, 2005, IMPAX gave Biovail notice of its Paragraph IV Certification filed with its amendment to ANDA 77-415 which sought approval of its 300 mg tablet (300 mg Notice). Id. Biovail received the 300 mg Notice on January 26, 2005.

On March 7, 2005, 42 days after Biovail received the 150 mg Notice, it filed a patent infringement suit in the Eastern District of Pennsylvania. See Complaint for Patent Infringement in Biovail Labs., Inc. v. IMPAX Labs., Inc., No. 05-cv-1085 (E.D. Pa.), Dkt. No. 1. The Complaint stated that it was an action against IMPAX for its filing of ANDA 77-415 "for Buproprion Hydrochloride 150 mg extended release tablets (IMPAX's 150 mg Buproprion XL tablets)." Id. ¶ 1 (emphasis added). The Complaint further referenced a notice letter dated January 20, 2005, in which IMPAX advised Biovail that it had filed ANDA 77-415 "for Buproprion Hydrochloride 150 mg extended release tablets." Id. ¶¶ 1, 12 (emphasis added).[3]

On April 7, 2005, 72 days after receiving the 300 mg Notice, Biovail amended its patent infringement case against IMPAX. See Amended Complaint in Biovail Labs., Inc. v. IMPAX Labs., Inc., No. 05-cv-1085 (E.D. Pa.), Dkt. No. 4. The Amended Complaint stated that it was an action against IMPAX's filing of ANDA 77-415 "and amendments thereto" "for Buproprion Hyrochloride 150 mg and 300 mg extended release tablets (IMPAX's 150 mg Bupoprion XL tablets and IMPAX's 300 mg Buproprion XL tablets)." Id. ¶ 1 (emphasis added). The Amended Complaint further referenced for the first time, the second notice letter, and referred to the "Notice Letters" dated January 20, 2005 and January 24, 2005, notifying Biovail that IMPAX had filed an ANDA with FDA for the 150 and 300 mg extended release tablets. Id. ¶ ¶ 1, 12.[4]

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[3] On March 16, 2005, IMPAX, in accordance with 21 C.F.R. § 314.107(f)(2), notified FDA that "Biovail Laboratories, Inc. initiated a lawsuit for the 150 mg strength only, within the 45-day period as provided for in section 505(j)(4)(B)(iii) [sic] of the [FDCA]." See Exh. 4 (emphasis in original).

[4] By letter dated April 21, 2005, IMPAX notified FDA that Biovail had amended its patent infringement complaint to include the 300 mg strength. See Exh. 5. IMPAX further stated: "Please note that the amended complaint was filed on April 7, 2005, following the expiration of the 45-day period as provided for in section 505(j)(4)(B)(iii) of the [FDCA]." Id.

ARGUMENT

A preliminary injunction is an extraordinary remedy for which the plaintiff bears the burden of proving the prerequisites by clear and convincing evidence. Granny Goose Foods, Inc. v. Brotherhood of Teamsters, 415 U.S. 423, 441 (1974); see also Direx Israel, Ltd. v. Breakthrough Med. Corp., 952 F.2d 802, 812 (4th Cir. 1992). "Preliminary injunctions are extraordinary remedies involving the exercise of very far-reaching power to be granted only sparingly and in limited circumstances." In re Microsoft Corporation Antitrust Litigation, 333 F.3d 517, 524 (4th Cir. 2003) (reversing district court's grant of a preliminary injunction) (quotation marks omitted). Before issuing a preliminary injunction, a court "must consider (1) the likelihood of irreparable harm to the plaintiff if the preliminary injunction is denied; (2) the likelihood of harm to the defendant if the request is granted; (3) the likelihood that the plaintiff will succeed on the merits; and (4) the public interest." Microstrategy, Inc., 245 F.3d 335, 339 (4th Cir. 2001); see also Blackwelder Furniture Co. v. Seilig Mfg. Co., 550 F.2d 189, 193-95 (4th Cir. 1977).

A court must determine whether the plaintiff has made a strong showing of irreparable harm if the injunction is denied; if such a showing is made, the court must then balance the likelihood of harm to the plaintiff against the likelihood of harm to the defendant. Scotts Co. v. United Indus. Corp., 315 F.3d 264, 271 (4th Cir. 2002). As the balance of hardships becomes substantially equal between the plaintiff and defendant, the probability of success assumes more significance, and interim relief requires a clearer showing of a likelihood of success on the merits. Id. Here, Biovail has failed to establish either irreparable harm or that it is likely to succeed on the merits. Biovail's request for the extraordinary remedy of a preliminary injunction

should be denied.

I. BIOVAIL IS UNLIKELY TO SUCCEED ON THE MERITS BECAUSE FDA'S APPROVAL OF THE 300 mg DOSAGE OF BUPROPRION UNDER ANDA 77-415 WAS REQUIRED BY THE STATUTE

Biovail's request for temporary injunctive relief should be denied because it is unlikely to succeed on the merits. Biovail failed to file its infringement suit with respect to the 300 mg strength drug product within the 45 day time frame required by the FDCA to obtain a 30 month stay, 21 U.S.C. § 355(j)(2)(A)(vii), and therefore, approval of IMPAX's ANDA for the 300 mg dosage was not only proper, but required by law. Id. ("approval shall be made effective immediately"). Approval is only delayed when an action for infringement against that particular drug product has been filed within 45 days after the date of receiving a Paragraph IV certification. Id. In the present case, Biovail did not bring an action for infringement against IMPAX for its 300 mg drug until 72 days after receiving notice of the Paragraph IV certification for the 300 mg product and, thus, is not entitled to the 30 month stay under the statute.

Nor did Biovail's timely filing of a patent infringement action against IMPAX's 150 mg drug product stay approval of IMPAX's 300 mg drug product. Biovail incorrectly argues that FDA's approval of IMPAX's 300 mg drug product "fails at the first step of the Chevron analysis." PI Mem. at 11. FDA's approval of IMPAX's 300 mg drug product was based on the statutory language in 21 U.S.C. § 355(j)(2)(A)(vii) , as well as its long-standing and publicly noticed interpretation that a drug product is defined by the active ingredient, dosage form, strength, and route of administration (see e.g., 21 C.F.R. § 314.3, 54 Fed. Reg. 28872, 28877 (Jul. 10, 1989) (preamble to ANDA regulations, and Shimer (attached at Exh. 1)), and Biovail's failure to timely sue for patent infringement on the 300 mg drug product.

Under the two-step test of Chevron, U.S.A Inc v. Natural Resources Defense Council, Inc., 467 U.S. 837, (1984), the court's first inquiry is whether the intent of Congress is clear. If so, no further inquiry is required. If the statute is silent or ambiguous, however, the court's inquiry is whether the agency's position is based on a permissible construction of the statute. Id. at 843. FDA prevails under both prongs of Chevron analysis.

Step One of the Chevron Analysis

The FDCA reflects Congress's intent that FDA's approval of a generic drug product be specific to, among other things, a particular strength of a drug. See 21 U.S.C. § 355(j)(2). The FDCA states that an ANDA for a new drug shall contain, among other things: "(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug . . . or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed . . ., such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require" and "(iv) information to show that the new drug is bioequivalent to the listed drug . . . ." 21 U.S.C. § 355(j)(2)(A) (emphasis added). It is clear, therefore, that ANDA applicants who seek to market generic drugs must seek approval for each strength of the drug product it seeks to market and each ANDA applicant must include certifications for each patent that "claims the listed drug" or "a use for such listed drug for which the applicant is seeking approval." 21 U.S.C. § 355(j)(2)(A)(vii) (emphasis added).

FDA's regulations define "drug product" as "a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association

with one or more other ingredients." 21 C.F.R. § 314.3(b). Further, the regulations define "listed drug" as "a new drug product that has an effective approval under section 505(c) of the [FDCA] for safety and effectiveness or under section 505(j) of the [FDCA] . . . . Listed drug status is evidenced by the drug product's identification as a drug with an effective approval in the current edition of FDA's 'Approved Drug Products with Therapeutic Equivalence Evaluations' (the list) or any current supplement thereto, as a drug with an effective approval. A drug product is deemed to be a listed drug on the date of effective approval of the application or abbreviated application for that drug product." Id.

It is hardly surprising, therefore, that the patent certifications required by 21 U.S.C. § 355(j)(2)(A)(vii) also must be specific to the listed drug product for which approval is being sought. The statute requires that an ANDA must contain a "certification, the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause . . . or which claims a use for such listed drug for which the applicant is seeking approval under this subsection . . . ." 21 U.S.C. § 355(j)(2)(A)(vii). Thus, the FDCA requires separate patent certifications for each listed drug. Notably, drugs are listed by strengths. See e.g., Shimer Dec at Exh.1

Under the FDCA, if an ANDA applicant files a Part IV certification (as IMPAX did herein), "the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) before the date on which the application (excluding an amendment or supplement to the application) was

submitted." 21 U.S.C. § 355 (c)(3)(C).

Thus, approval under an ANDA for one strength of a drug does not, and cannot under the explicit terms of the statute, apply to other drug products with different strengths. Accordingly, under step one of the Chevron analysis, FDA can neither approve a drug product under an ANDA for a different strength than that for which the patent certification has been filed, nor delay approval of a drug product based on a certification, unless a timely patent infringement action has been filed that pertains to that exact drug product.

In this case, Biovail filed its patent infringement lawsuit on the 150 mg product within the 45 days required under the FDCA, but it did not file its lawsuit on the 300 mg product within the required timeframe. Thus, IMPAX's 300 mg product is eligible for approval, and once scientific hurdles were cleared, FDA's approval of it was required by the FDCA. As the court held in Mylan Labs. v. Thompson, 389 F.3d 1272, 1284 (D.C. Cir. 2004) ("if the patent holder fails to [promptly file an infringement action" within forty-five days, it will lose the benefit of the 30-month stay period").

Step Two of the Chevron Analysis

Even assuming that the statute did not dictate FDA's approval of IMPAX's 300 mg drug product in the present case, FDA's action was permissible under the statute and thus should be upheld under Chevron step two. See, e.g., Watson Pharmaceuticals, Inc. v. Henney, 194 F. Supp.2d 442, 445 (D. Md. 2001) ("The judicial deference owed the agency in interpretation of its own governing statutes and regulations is especially great.") (citing Chevon, U.S.A., Inc. v. Natural Resources Defense Council, Inc., 467 U.S. 837, 844-45 (1984)).

FDA's longstanding interpretation, in a variety of contexts, has been that, even when the

active ingredients are the same, variations in route of administration, dosage form, and strength create different drug products. The Supreme Court has made clear that the "new drug" definition is to be interpreted broadly. See, e.g., United States v. Generix Drug Corp., 460 U.S. 453, 461 (1983) (even a drug product containing the same active ingredient as an FDA-approved drug product but different inactive ingredients is a "new drug"); USV Pharm. Corp. v. Weinberger, 412 U.S. 655, 664 (1973) (even a drug that is identical to an approved drug is a "new drug" that must be independently established as safe and effective if it is produced by a different manufacturer). See Shimer Dec. at Exh. 1.

In Pfizer v. Food and Drug Administration, 753 F. Supp. 171 (D. Md. 1989), this Court accepted FDA's treatment of a soft gelatin capsule as a different product than a tablet formulation with the same active ingredient for purpose of patent listing. And, in Apotex v. Shalala 53 F. Supp.2d 454 (D.D.C. 1999), aff'd Apotex, Inc. v. Shalala, 1999 WL 956686 (D.C.Cir. Oct 8, 1999), the District Court for the District of Columbia upheld FDA's determination that 150 mg and 300 mg dosages a drug were separate drug products for purposes of 180 day marketing exclusivity. The Court upheld FDA's practice of granting exclusivity periods for specific drug products, as they relate to certain patents under both Chevron steps one and two. Id. Citing FDA's brief, the Court explained that FDA's interpretation of the statute is permissible in light of the statute, the purposes of Hatch Waxman, and FDA's role in the ANDA approval process:

> [a] decision of a court that one strength of a product does not infringe a patent cannot automatically mean that a different strength also does not infringe. Different strengths of the same drug may be formulated differently for a variety of reasons, and varying formulations of the different strengths may provide separate and distinct bases for patent protection or for patent

challenges.

53 F. Supp. 2d 454 at 463 (emphasis added.).

Biovail's argument that its patent lawsuit alleging infringement, specifically relating to IMPAX 150 mg tablets (See Complaint ¶ 12), should stay approval of IMPAX 300 mg tablets is untenable, for at least two reasons. First, it requires analysis of the merits of complicated patent cases that FDA does not have either the resources or expertise to assess, and that it is not required to possess under the law. See Watson Pharmaceuticals, 194 F. Supp.2d at 445 ("the legislation clearly reflects that Congress recognized that the FDA had a very limited ministerial role in patent fights between patentees and generic marketers") See also 54 Fed. Reg. 28,872, 28,888 (July 10, 1989); 59 Fed. Reg. at 50,342-43, 50,349, 50,352 (October 3, 1994). The statute should not be read to require such action by FDA and FDA's contrary interpretation is a permissible reading of the statute. See Watson Pharmaceuticals, 194 F. Supp.2d at 445 (noting that FDA "has no expertise – much less any statutory franchise – to determine matters of substantive patent law").

Moreover, in the present case, to accept Biovail's argument would require not only that FDA delve into these complicated patent cases, but that when it does so that it interpret a complaint that makes allegations about a specific product (in this instance 150 mg tablets) to include some indeterminate scope of other drug products, including at least a 300 mg tablet strength that Biovail was fully aware of when it filed its complaint but which was conspicuously absent from the otherwise specific allegations of its complaint regarding the 150 mg strength. In addition to being illogical, this argument would also undercut the competition the Hatch Waxman amendments sought to foster, whereas FDA's interpretation of the statute, making

generic approval under ANDAs specific to each particular strength of drug, serves the important goal of promoting generic competition.

Accordingly, Biovail is unlikely to succeed on the merits, and thus its request for temporary relief should be denied on that grounds alone.

II. BIOVAIL HAS NOT SHOWN THAT IT WILL SUFFER IRREPARABLE HARM ABSENT PRELIMINARY INJUNCTIVE RELIEF

Biovail has failed to demonstrate that it will suffer irreparable harm absent injunctive relief or that the balance of hardships tips in its favor. Courts insist that only *irreparable* harm justifies the issuance of a preliminary injunction. Hughes Network Systems v. Interdigital Communications Corp., 17 F.3d 691, 694 (4th Cir. 1994). Indeed, "[t]he *sine qua non* of granting any preliminary injunctive relief is a clear and convincing showing of irreparable injury to the plaintiff." Experience Works, Inc. v. Chao, 267 F. Supp. 2d 93, 96 (D.D.C. 2003). Irreparable injury is a "very high standard." See Varicon Int'l v. OPM, 934 F. Supp. 440, 447 (D.D.C. 1996); Bristol-Myers Squibb Co. v. Shalala, 923 F. Supp. at 220. The injury alleged must be certain, great, actual, and imminent, Wisconsin Gas Co. v. FERC, 758 F.2d 669, 674 (D.C. Cir. 1985), and it must be "more than simply irretrievable; it must also be serious in terms of its effect on the plaintiff." Mylan v. Thompson, 139 F. Supp. 2d 1, 27 (D.D.C.), rev'd other grounds, 268 F.3d 1323 (Fed. Cir. 2001) (quoting Gulf Oil Corp. v. Dept. of Energy, 514 F. Supp. 1019, 1026 (D.D.C. 1981)).

It is well settled that mere economic loss in and of itself does not constitute irreparable harm. Wisconsin Gas, 758 F.2d at 674; Mylan Pharms., Inc. v. Thompson, 207 F. Supp. 2d 476, 485 (N.D. W. Va. 2001); Boivin v. US Airways, Inc., 297 F. Supp. 2d 110, 118 (D.D.C. 2003);

Mylan Pharm., Inc. v. Shalala, 81 F. Supp. 2d 30, 42 (D.D.C. 2000); Bristol-Myers, 923 F. Supp. at 220. "Mere injuries, however substantial, in terms of money, time and energy necessarily expended" are inadequate. Wisconsin Gas, 758 F.2d at 674 (quoting Virginia Petroleum Jobbers Ass'n v. FPC, 259 F.2d 921, 925 (D.C. Cir. 1958)). Even irrecoverable economic loss does not rise to the level of irreparable harm unless the financial injury is so great as to "cause extreme hardship to the business, or even threaten destruction of the business." Gulf Oil, 514 F. Supp. at 1025; see also Experience Works, 267 F. Supp. 2d at 96 ($21.1 million reduction in funding is serious financial blow, but one frequently faced by other similar entities, and not an economic loss that threatens survival of the business); Sociedad Anomia Vina Santa Rita v. Dep't of Treasury, 193 F. Supp. 2d 6, 14 (D.D.C. 2001) ("financial harm alone cannot constitute irreparable injury unless it threatens the very existence of the movant's business").

Notwithstanding this well-established doctrine, economic loss is precisely the type of harm that Biovail alleges it will suffer in the absence of a preliminary injunction. See PI Mem. at 11-13. Specifically, Biovail asserts that the introduction of a generic Wellbutrin XL "could cause Biovail to lose hundreds of millions of dollars of product revenue in the first 12 months," with an estimated loss of approximately 60 to 65 percent of its total revenue base. See Howling Decl., ¶¶ 10, 11. Biovail further states that it is a "relatively small company in which Wellbutrin XL . . . is a significant percentage of [its] business. Id. ¶ 13. Biovail, however, makes no attempt to document the actual impact of this lost revenue on its financial bottom line, nor does it differentiate between its revenue from sales of 150 mg Wellbutrin XL and sales of its 300 mg

dosage.[5]

Biovail's representations before this Court differ from the representations it made in the Form 6-K it filed with the Securities and Exchange Commission (SEC) for the quarterly period ended June 30, 2006. Attached at Exh. 6. There, Biovail represented the SEC that "[s]ince its launch by [GSK] . . . in September 2003, through to June 30, 2006, Wellbutrin XL® has accounted for approximately 40 percent overall of [Biovail's] consolidated revenue from product sales.

Furthermore, Biovail is by no means a one-product company. Cf. Bracco Diagnostics, Inc. v. Shalala, 963 F. Supp. 20, 29 (D.D.C. 1997) (recognizing injury to one-product line company). Biovail is not a one drug product company and markets a wide variety of other products as well. Moreover, only a portion of Biovail's sales would be lost to generic competition, which reduces that small percentage even more. Additionally, there is no reason to expect that Biovail's sales will be eliminated. It will still retain some share of the marketplace, especially for its 150 mg dosage. .

Biovail asserts that its losses are irreparable because they are unrecoverable from the government. PI Mem. at 12. Here, too, Biovail's assertion is flawed. Although Biovail has a patent sui pending against IMPAX, Biovail speculates that it faces a "significant risk" that it "could be barred from recovering damages against Impax." PI Mem. at 12. In support of this argument, Biovail cites only Mylan Pharms, Inc. v. Shalala , 81 F. Supp. 2d 30 (D.D.C. 2000).

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[5] Even if IMPAX markets the generic 300 mg Wellbutrin XL, Biovail will continue to have a viable market for its 150 mg dosage products. These are extended release tablets, so patients could not simply buy the generic 300 mg dosage and cut them in half to obtain the same effect as the 150 mg dosage tablet.

Id. Mylan Pharms is readily distinguishable from the present case. In that action, the court found that Mylan's delay in bringing suit undercut its irreparable injury argument. 81 F. Supp. 2d at 44-45. The holding in Mylan Pharms. in no way suggests that Biovail will be barred from recovering damages in its underlying patent dispute pending in the Eastern District of Pennsylvania. If Biovail wins in Pennsylvania, it will recover damages there. If it loses in Pennsylvania, it is not entitled to money there, or an injunction here. Moreover, Biovail cites to nothing in its patent case that suggests that its right to recover damages in that action will in any way be affected by this Court's ruling that Biovail failed to timely bring suit for purposes of obtaining a 30 month stay against Impax 300 mg drug product. Thus, the alleged lost sales that may result from competition with a generic version of its 300 mg Wellbutrin XL do not constitute irreparable harm.

Biovail's attempt to meet the irreparable harm standard is further weakened by its own statement in its SEC filing that, "[i]n the event of generic competition, GSK may launch an authorized generic version of Wellbutrin XL® for distribution in the U.S. Under the terms of the Wellbutrin XL® agreement, [Biovail] will be the exclusive manufacturer and supplier to GSK of such an authorized generic. [Biovail's] supply price to GSK for Wellbutrin XL® generic product will be fixed each year based on contractually agreed prices. This supply price will be substantially lower than the tiered supply price that [Biovail] currently receives on sales of Wellbutrin XL® brand product." See Exh. 6 . The impact of generic Wellbutrin competition cannot constitute irreparable harm in view of both the non-substantial impact of lost Wellbutrin 300 mg sales on Biovail's total sales picture and the profits that Biovail will gain by supplying an "authorized generic."

Finally, any financial harm that Biovail may suffer in the absence of preliminary injunctive relief will be matched, if not exceeded, by the financial harm that generic manufacturer IMPAX will suffer by being wrongfully deprived of its right to market a competing generic product during the period that a preliminary injunction is in effect. In Glaxo v. Heckler, 623 F. Supp. 69 (E.D.N.C. 1985), when Glaxo sought a preliminary injunction to prevent approval of a generic, the court held: "Glaxo cannot show that any injury it suffers without a decree outweighs Lilly's injury suffered by issuance of such a decree." Id. at 71. Also, the Court stated: "In considering the probable injury to Glaxo without a decree and the likely harm to the FDA and Lilly with a decree, it is clear that a balance has not been struck in Glaxo's favor." Id. at 73. See also Serono, 158 F.3d at 1326; Bristol-Myers, 923 F.Supp. at 221. For all of these reasons, Biovail cannot meet its burden of establishing that it will suffer irreparable injury in the absence of preliminary injunctive relief, or that the balance of hardships weighs in its favor.

Courts insist that only irreparable harm justifies the issuance of a preliminary injunction. Hughes, 17 F.3d at 694. Because Biovail has failed to satisfy its burden of demonstrating either irreparable harm or that the balance of harms weighs in its favor, "the probability of success begins to assume real significance, and interim relief is more likely to require a clear showing of a likelihood of success." Direx, 952 F.2d at 808. Biovail has completely failed to demonstrate that it is likely to succeed on the merits, for all of the reasons stated in Section I, supra. Thus, Biovail has failed to demonstrate that this case warrants the grant of the extraordinary remedy of a preliminary injunction.

III. FDA WILL BE HARMED IF BIOVAIL'S REQUEST FOR RELIEF IS GRANTED

Biovail has also failed to show that any harm it may suffer in the absence of injunctive relief outweighs the potential harm to FDA and the public. Although FDA has no commercial stake in the outcome of this litigation, FDA is the government agency charged with implementing the statutory scheme governing the approval of generic drugs. As such, FDA's interest coincides with the public interest. Serono Labs, Inc. v. Shalala,158 F.3d at 1326 (D.C. Cir. 1998); Mylan Pharms., Inc. v. Shalala, 81 F. Supp. 2d at 41-45.

Biovail argues that FDA will suffer no cognizable harm if a preliminary injunction "on account of its violations of its own regulations and due process." PI Mem. at 13. Biovail ignores, however, that the agency has already determined pursuant to its statutory authority that the 300 mg generic Wellbutrin XL product at issue is safe, effective, and ready for approval and distribution to the public. A preliminary injunction, therefore, would thwart Congress's generic drug approval scheme and FDA's lawful implementation of that scheme by forcing FDA to suspend its approval of what FDA considers to be an *approved* ANDA.

Biovail also argues that IMPAX would not suffer any cognizable harm if a preliminary injunction issues because "IMPAX has no entitlement, or realistic expectation, to bring its product to the market until the expiration" of the 30-month stay period. PI Mem. at 13. This is simply untrue. From the start of Biovail's patent infringement litigation, IMPAX has believed that the 30-month stay period applies only to its 150 mg dosage of generic Wellbutrin XL, because Biovail failed to include the 300 mg dosage in its patent infringement complaint within the 45-day timeframe set forth in the FDCA.[6] IMPAX had a reasonable expectation that there

[6] Biovail makes much of IMPAX's SEC filing that discussed the patent lawsuit. See PI Mem. at 7. Biovail's conclusion that "IMPAX's SEC filing recognized that the suit applied to both dosages" is wrong. Id. IMPAX's filing with the SEC simply states that Biovail has filed a

was no 30-month stay on the marketing of IMPAX's 300 mg generic product, and that IMPAX could go to market immediately upon FDA approval.

A court-ordered delay of approval of a lawfully approved drug, however, is qualitatively very different from any delay in market entry pending FDA's review of an ANDA. A court-ordered delay of approval would directly undermine FDA's interest in approving safe and effective generic drugs and making those drugs available to the public, whereas the review period for an ANDA ensures the public of the integrity of the drugs that are approved. Once FDA approves a drug, any continued delay in approval may be justified only in extreme circumstances not present here. See Direx, 952 F.2d at 811 ("A preliminary injunction is, however, an 'extraordinary remedy'" that should be granted "only in the limited circumstances which clearly demand it.").

The public and FDA would therefore be considerably harmed if this Court were to grant a preliminary injunction. For these reasons, the balance of harms do not tilt decidedly in Biovail's favor.

IV. THE PUBLIC INTEREST WEIGHS AGAINST BIOVAIL'S REQUEST FOR INJUNCTIVE RELIEF

FDA's interest and the public's interest in generic drug approvals are the same. See Serono, 158 F.3d at 1326 (determining that the public interest is "inextricably linked" to Congress's purpose in passing the Hatch-Waxman Amendments). FDA must implement the

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lawsuit against IMPAX "related to IMPAX's filing for a generic version of Wellbutrin XL." See Exh. 4 to PI Memo at p.56. The filing further states that IMPAX filed Paragraph IV Certifications with FDA stating that it believes that its 150 mg and 300 mg versions of the drugs do not infringe Biovail's listed patents. In no way does this filing show that IMPAX was on notice that the lawsuit applied to both the 150 and 300 mg dosages.

statutory scheme governing the approval of generic drugs to make lower cost drugs available to the public when those drugs are found to meet the requirements for approval. See In re Barr Laboratories, Inc., 930 F.2d 72,76 (D.C. Cir. 1991) ("Congress sought to get generic drugs into the hands of patients at reasonable prices - fast.").

For the reasons stated above, FDA has determined that IMPAX's 300 mg generic Wellbutrin has met the statutory requirements for approval. The public benefits from the increased competition incident to FDA's approval of a generic version of 300 mg Wellbutrin. The public interest, therefore, weighs against Biovail's claim for injunctive relief.

Biovail misplaces its reliance on Mova Pharm. Corp. v. Shalala, 955 F. Supp. 128, 131 (D.D.C. 1997) for the proposition that the public's interest in generic drug entry does not outweigh the interest in an agency's correct application of the law. PI Mem. at 14. In Mova, the court issued an injunction where there was a high likelihood of Mova's eventual success on the merits. 955 F. Supp. 128 at 131. On appeal, the D.C. Circuit affirmed an injunction where the factors other than the merits were not seriously contested, and where all of the factors other than the public interest weighed heavily in favor of granting another injunction. Mova Pharm. Corp. v. Shalala, 140 F.3d 1060, 1066 n.6 (D.C. Cir. 1998). In such circumstances, the court noted that "this factor alone [the public interest in generic drug entry] cannot support denying an injunction." Here, where FDA is likely to succeed on the merits, and where Biovail does not face irreparable harm, the public interest calculus is very different, and weighs against an injunction.

CONCLUSION

For the foregoing reasons, Biovail's motion for a temporary restraining order and preliminary injunction should be denied.

Respectfully submitted,

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